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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,515	08/07/2001	Rosanne M. Crooke	ISPH-0595	1714

36441 7590 11/03/2004

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,515	CROOKE ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *August 11, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignments*.

DETAILED ACTION

This Office Action is a response to Applicants Amendment and Remarks filed August 11, 2004.

Claims 1 and 11 have been amended. Claims 1, 2, and 4-15 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

Applicant's information disclosure statement, filed August 11, 2004 is acknowledged. The information referred to therein has been considered on the merits.

Claim Objections

In the previous Office Action mailed March 9, 2004, claim 1 was objected to because it contained a typographical error. **This objection is withdrawn** in view of Applicants Amendment to correct for the typographical error.

Claim Rejections - 35 USC § 102

In the previous Office Action mailed March 9, 2004, claims 1, 2, 11, 12, 14, and 15 were rejected under 35 USC 102(b) as being anticipated by Morishita et al. (Circulation, 1998 Vol. 98:1898-1904). **This rejection is withdrawn** in view of Applicants amendment to the claims to recite an antisense compound 12 to 30 nucleobases in length targeted to a nucleic acid molecule encoding human apolipoprotein (a). Specifically, this rejection is withdrawn because Morishita et al. disclose three phosphorothioate backbone ribozyme oligonucleotides, 42-base pairs in length targeted to kringle 4 of the human apolipoprotein (a).

Claim Rejections - 35 USC § 103

In the previous Office Action mailed March 9, 2004, claims 1, 2, 4, 5, 6-10 and 12-14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Morishita et al. (Circulation, 1998 Vol. 98:1898-1904) in view of Baracchini et al. [U.S. Patent No. 5801154] and Fritz et al. (Journal of Colloid and Interface Science, 1997 Vol. 195:272-288). **This rejection is withdrawn** in view of Applicants amendment to the claims to recite an antisense compound 12 to 30 nucleobases in length targeted to a nucleic acid molecule encoding human apolipoprotein (a). Specifically, this rejection is withdrawn because Morishita et al. disclose three phosphorothioate backbone ribozyme oligonucleotides, 42-base pairs in length targeted to kringle 4 of the human apolipoprotein (a).

The following are new rejections:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 4-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Bennett et al. [U.S. Patent No. 6,008,344].

Claim 1 is drawn to a compound 12 to 30 nucleobases in length targeted to a nucleic acid molecule encoding human apolipoprotein (a); wherein said compound specifically hybridizes with said nucleic acid molecule encoding human apolipoprotein (a) and inhibits the expression of human apolipoprotein. Claims 2-10 are dependent on claim 1, and include all the limitations of claim 1, with the further limitations, wherein the compound is an antisense oligonucleotide, wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage, wherein the modified internucleoside linkage is a phosphorothioate linkage, at least one modified sugar moiety, wherein the modified sugar moiety is a 2-O-methoxyethyl sugar moiety, at least one modified nucleobase, wherein the modified nucleobase is a 5-methylcytosine, wherein the antisense oligonucleotide is a chimeric oligonucleotide. Claim 11 is drawn to a compound 12 to 30 nucleobases in length that specifically hybridizes with at least an 8-nucleobase portion of an active site on a nucleic acid encoding human apolipoprotein (a). Claims 12-14 are drawn to a an antisense compound 12 to 30 nucleobases in length targeted to a nucleic acid molecule encoding

human apolipoprotein (a), wherein said compound specifically hybridizes with at least an 8-nucleobase portion of an active site on a nucleic acid molecules encoding human apolipoprotein (a), and further comprising a pharmaceutically acceptable carrier, diluent, or colloidal dispersion system, wherein the compound is an antisense oligonucleotide. Claim 15 is drawn to a method of inhibiting the expression of human apolipoprotein (a) in cells or tissues comprising administering a compound 12 to 30 nucleobases in length targeted to a nucleic acid molecule encoding human apolipoprotein (a); wherein said compound specifically hybridizes with said nucleic acid molecule encoding human apolipoprotein (a) and inhibits the expression of human apolipoprotein.

Bennett et al. disclose a modified antisense oligonucleotide targeted to phospholipase A2 group IV with the following sequence: 5'-atagcactccttcagccc-3' (see SEQ ID NO:43). Bennett et al. further disclose that the antisense oligonucleotide targeted to phospholipase A2 group IV was effective *in vitro* (see Table 2). This antisense oligonucleotide is reverse complementary to bases 457-473 of SEQ ID NO:3 of the instant invention. It is noted that the reverse complimentarity between the antisense oligonucleotide targeted to phospholipase A2 group IV disclosed by Bennett et al. and nucleobases 457-473 of SEQ ID NO:3 is not contiguous. However, the antisense oligonucleotide targeted to phospholipase A2 group IV disclosed by Bennett et al. exhibits almost 89% local similarity to nucleobases 457-473 of SEQ ID NO:3 of the instant invention, as it contains two mismatches (see attached sequence alignment). Given this high degree of similarity, the antisense oligonucleotide targeted to phospholipase A2 group IV disclosed by Bennett et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" with a nucleic acid molecule encoding human

apolipoprotein (a) as defined in the instant specification at page 8, lines 31-35 and page 9, lines 1-13. Accordingly, the antisense oligonucleotide disclosed by Bennett et al. would specifically hybridize to bases 457-473 of SEQ ID NO:3 as claimed.

The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the modified antisense oligonucleotide disclosed by Bennett et al. would or would not have the additional functional limitation of "inhibiting expression" of human apolipoprotein (a) under generally any assay conditions.

Therefore, absent evidence to the contrary, claims 1, 2, and 4-15 are anticipated by Bennett et al.

Claims 1, 2, 11, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Baker et al. [U.S. Patent No. 6,080,580].

Baker et al. disclose a TNF-α PCR primer with the following sequence: 5'-CAGGCGGTGCTTGTTCCT-3' (see SEQ ID NO:43). This PCR primer is reverse complementary to bases 430-445 of SEQ ID NO:3 of the instant invention. It is noted that the reverse complimentarity between the TNF-α PCR primer disclosed by Bennett et al. and nucleobases 430-445 of SEQ ID NO:3 is not contiguous. However, the TNF-α PCR primer disclosed by Bennett et al. exhibits almost 94% local similarity to nucleobases 430-445 of SEQ ID NO:3 of the instant invention, as it contains only one mismatch (see attached sequence alignment). Given this high degree of similarity, TNF-α PCR primer disclosed by Bennett et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" with a nucleic acid molecule encoding human apolipoprotein (a) as defined in the instant specification at page 8, lines 31-35 and page 9, lines 1-13. Accordingly, the TNF-α PCR primer disclosed by Bennett et al. would specifically hybridize to bases 430-445 of SEQ ID NO:3 as claimed.

The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658

(Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the TNF-α primer disclosed by Baker et al. would or would not have the additional functional limitation of "inhibiting expression" of human apolipoprotein (a) protein under generally any assay conditions.

Therefore, absent evidence to the contrary, claims 1, 2, 11, 12, and 14 are anticipated by Baker et al.

Claims 1, 2, 11, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by McLean et al. Nature, 1987 Vol. 330:132-137.

McLean et al. disclose a synthetic 30-base oligonucletoide that spanned the breakpoint of apo(a) and plasminogen similarity in the signal peptide region (see Figure 1b at dotted underline). This synthetic oligonucleotide is reverse complementary to bases 80-109 of SEQ ID NO:3 of the instant invention. It is noted that the reverse complimentarity between the synthetic oligonucleotide disclosed by McLean et al. and nucleobases 80-109 of SEQ ID NO:3 is contiguous. Given this high degree of similarity, the synthetic oligonucleotide disclosed by McLean et al. meets the structural limitations of the claimed invention and would be expected to

"specifically hybridize" with a nucleic acid molecule encoding human apolipoprotein (a) as defined in the instant specification at page 8, lines 31-35 and page 9, lines 1-13.

The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the synthetic oligonucleotide disclosed by McLean et al. would or would not have the additional functional limitation of "inhibiting expression" of human apolipoprotein (a) protein under generally any assay conditions.

Therefore, absent evidence to the contrary, claims 1, 2, 11, 12, and 14 are anticipated by McLean et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLean et al. Nature, 1987 Vol. 330:132-137, in view of Morishita et al. (Circulation, 1998 Vol. 98:1898-1904), and Baracchini et al. [U.S. Patent No. 5,801,154], and McKay et al. [U.S. Patent No. 6,258,601].

Claims 1, 2, and 4-15 are drawn to an antisense oligonucleotide 12 to 30 nucleobases in length targeted to a nucleic acid molecule encoding human apolipoprotein (a); wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage; wherein the modified internucleoside linkage is a phosphorothioate linkage; wherein the antisense oligonucleotide comprises at least one modified sugar moiety; wherein the sugar moiety is a 2'-O-methoxyethyl sugar moiety; wherein the antisense oligonucleotide comprises at least one modified nucleobase; wherein the modified nucleobase is a 5-methylcytosine; wherein the antisense oligonucleotide is a chimeric oligonucleotide; and a composition comprising an antisense oligonucleotide 12 to 30 nucleobases in length targeted to a nucleic acid molecule encoding human apolipoprotein (a) and a pharmaceutically acceptable carrier or diluent, further comprising a colloidal dispersion system. The claims are further drawn to methods to inhibit the expression of human apolipoprotein (a) in cells *in vitro*.

McLean et al. teaches the full-length sequence of human apolipoprotein (a) as represented in SEQ ID NO:3 of the instant invention (see McLean et al. Figure 1). McLean et al. do not teach antisense targeted to apolipoprotein (a), including antisense with a length of 12 to 30 nucleobases. McLean et al. also do not teach antisense targeted to a nucleic acid encoding apolipoprotein (a) wherein the antisense comprises modified internucleoside linkages or wherein the antisense is a chimeric antisense molecule.

Morishita et al. teach three phosphorothioate backbone ribozyme oligonucleotides, 42-base pairs in length targeted to kringle 4 of the human apolipoprotein (a) (see page 1899, Methods and Figure 1A). Morishita et al. also teach that the expression of ribozymes targeting human apolipoprotein (a) inhibited human apolipoprotein (a) protein expression in HepG2 cells (see Figures 2A and 2B), but not plasminogen concentrations (see Figure 3A). Morshita et al. do not teach antisense targeted to apolipoprotein (a) with a length of 12 to 30 nucleobases. Morshita et al. also do not teach antisense targeted to a nucleic acid encoding apolipoprotein (a) wherein the antisense comprises modified internucleoside linkages or wherein the antisense is a chimeric antisense molecule.

Baracchini et al. teach antisense of 12 to 30 nucleobases in length and teach modifications to antisense, including 2'-O'methoxyethyl sugar modifications, 5-methylcytosine base modifications, chimeric oligonucleotides and modified internucleoside linkages, including phosphorothioate linkages, to increase antisense stability and enhance affinity (see for example columns 6-9). Baracchini et al. further teach pharmaceutical carriers and colloidal dispersion systems (for example liposomes) for use in delivery of antisense compounds.

It would have been obvious to one of ordinary skill in the art to make an antisense oligonucletoide targeted to a nucleic acid encoding apolipoprotein (a) using the sequence taught by McLean and the motivation of Morshita et al. It would have been obvious to make a length within the range of 12 to 30 nucleobases (as taught by Baracchini et al.) because antisense of a short length are more easily synthesized and easier to deliver to cells. It would have been further obvious to make said antisense comprising modifications, including 2'-O'methoxyethyl sugar modifications, 5-methylcytosine base modifications, chimeric oligonucleotides and modified internucleoside linkages, including phosphorothioate linkages as taught by Baracchini et al, because such modifications were routine and well known in the art as modifications which enhance the stability, uptake and affinity of an antisense molecule, (see for example, Baracchini et al. column 6, paragraph 3).

It would have been obvious to one of ordinary skill in the art to make an antisense compound comprising antisense targeted to apolipoprotein (a) and a pharmaceutically acceptable carrier, including a colloidal dispersion system, because pharmaceutically acceptable carriers, including colloidal dispersion systems (e.g. liposomes) were well known in the art for use with antisense molecules as a means to deliver antisense molecules to cells *in vitro* (cell culture), as evidenced by Baracchini et al. Further, it would have been obvious to make an antisense compound targeted to apolipoprotein (a) because McLean et al. taught a human apolipoprotein (a) encoded by a nucleic acid comprising human apolipoprotein (a) of the instant invention and Morishita et al. teach generally making inhibitors to apolipoprotein (a). Although Morshita et al. teach ribozymes as specific inhibitors to apolipoprotein (a), the prior art teaches antisense oligonucleotides and ribozymes are art-recognized functional equivalents of each other. For

example, McKay et al. teach, "Antisense compounds include ribozymes" (see column 6, lines 5 and 6). Furthermore, the instant specification, at page 11, line 35 discloses, "Antisense compounds include ribozymes". Therefore it would have been obvious to substitute the ribozyme taught by Morishita et al. with the antisense oligonucleotide claimed in the instant invention since the two are functional equivalents of each other. See MPEP 2144.06.

One skilled in the art would have been motivated to make an antisense molecule targeted to a nucleic acid encoding apolipoprotein (a) because Morishita et al. explicitly teaches inhibiting the expression of apolipoprotein (a) using ribozyme nucleic acids and it is well known in the art that ribozyme is a means by which a target protein can be specifically targeted for functional studies and McLean et al. teach human apolipoprotein (a) as a protein to be studied and teach the full length sequence of a nucleic acid encoding human apolipoprotein (a). One of ordinary skill in the art would be motivated to make such antisense of a length within the rang of 12 to 30 nucleotides for ease of synthesis and delivery and because it is conventional in the art to make antisense within this size range (as exemplified by Baracchini et al.). One of ordinary sill would have been motivated to incorporate the modifications taught by Baracchini et al. into an antisense molecule targeted to apolipoprotein (a), for the benefits of stability and improved hybridization.

It would have been obvious to one of ordinary skill in the art to use antisense targeted to a nucleic acid encoding apolipoprotein (a) in a method of inhibiting the expression of apolipoprotein (a) in cells *in vitro* (cell culture) because Morishita et al. suggest using ribozymes targeted to apolipoprotein (a) to inhibit the expression of apolipoprotein (a) in cells *in vitro*, and

it would be an obvious use for an antisense molecule designed to hybridize to and inhibit the expression of a nucleic acid encoding human apolipoprotein (a).

Therefore, the invention of claims 1, 2, and 4-15 would have been obvious to one of ordinary skill in the art, as a whole, at the time the instant invention was made.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
October 27, 2004

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Sequence Alignment

Applicants Copy


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RESULT 96
AR100312/c
LOCUS       AR100312                 18 bp    DNA     linear   PAT 14-FEB-2001
DEFINITION  Sequence 43 from patent US 6080580.
ACCESSION   AR100312
VERSION     AR100312.1  GI:12810760
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 18)
  AUTHORS   Baker,B.F., Bennett,C.Frank., Butler,M.M. and Shanahan,W.R. Jr.
  TITLE     Antisense oligonucleotide modulation of tumor necrosis
            factor-.alpha. (TNF-.alpha.) expression
  JOURNAL   Patent: US 6080580-A 43 27-JUN-2000;
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              ||||||||||||| |||
Db         16 GAACAAGCACCGCCTG 1
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Sequence Alignment

Applicants Copy

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ACCESSION   AR096845
VERSION     AR096845.1  GI:10026010
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 18)
  AUTHORS   Bennett,C.Frank. and Cowsert,L.M.
  TITLE     Antisense modulation of phospholipase A2 group IV expression
  JOURNAL   Patent: US 6008344-A 43 28-DEC-1999;
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Qy         457 GGGGTGCAGGAGTGCTA 473
               ||| || ||||||||||
Db          18 GGGCTGAAGGAGTGCTA 2
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